

Non-Technical Abstract. Cystic fibrosis (CF) is the most common lethal hereditary disorder of Caucasians in the U.S. The major manifestations are in the lung, with thick, sticky mucus, chronic infections and inflammation. The average life span is approximately 28 years. The disease is caused by inherited abnormalities of the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Because of these genetic abnormalities, the cells lining the airways cannot move salt in a normal fashion, causing the mucus abnormalities, infection and inflammation and consequent progressive damage to the lung. In the context of laboratory studies demonstrating that transfer of the normal CFTR gene to the airway cells of individuals with CF will compensate for the abnormalities in the CFTR gene and permit airway cells to function in a normal fashion, this protocol is directed toward using a modified adenovirus to transfer the normal CFTR gene into the cells lining the airways of individuals with CF. Following a period of baseline evaluation, a defective adenovirus (which reduces the possibility of multiplication) will be instilled into the airways of individuals with CF. A variety of biologic and clinical parameters will be used to assess safety and biologic efficacy (the ability of the treatment to correct the abnormalities in the cells lining of the airways as assessed by laboratory tests). A total of 26 patients will receive the modified adenovirus, at various doses and time intervals. At the conclusion of this study, it should be possible to assess whether this strategy of compensating for the genetic abnormalities of CF will be a rational approach to treat the respiratory manifestations of this disease on a continuing basis.